

Cycloalkyl derivatives as bone resorption inhibitors and vitronectin receptor antagonists

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Abstract

Substituted cycloalkanes of formula $R<1>YABDEF'C(R<4>)(R<5>)(CH_2)_qR<9>$ (I) and their salts are new. A = bond, 1-8C alkanediyl, $NR<2>C(Q)NR<2>$, $NR<2>C(Q)Q$, $NR<2>S(O)nNR<2>$, $NR<2>S(O)nO$, $NR<2>S(O)n$, 3-12C cycloalkanediyl, C IDENTICAL C, $NR<2>CO$, $CONR<2>$, 5-14C arylene- $CONR<2>$, O, $S(O)n$, 5-14C arylene, CO, 5-14C arylene-CO, $NR<2>$, $SO_2NR<2>$, CO_2 , $CR<2>=CR<3>$ or 5-14C arylene- $S(O)n$ (all optionally mono- or disubstituted by 1-8C alkanediyl (sic), e.g. -1-8C alkanediyl- $CONR<2>$ -1-8C alkanediyl, 1-8C alkanediyl- $CONR<2>$ or $CONR<2>$ -1-8C alkanediyl); Q = O or S; B = bond, 1-10C alkanediyl, $CR<2>=CR<3>$ or C IDENTICAL C (all optionally mono- or disubstituted by 1-8C alkanediyl); D, F' = bond, 1-8C alkanediyl, or Q, $NR<2>$, $CONR<2>$, $NR<2>CO$, $NR<2>C(Q)NR<2>$, OCO, COO, CQ, $S(O)n$, $S(O)2NR<2>$, $NR<2>S(O)n$, $CR<2>=CR<3>$, C IDENTICAL C or $CH(OH)$ (all optionally mono- or disubstituted by 1-8C alkanediyl); E = 6-membered aromatic group optionally containing 1-4 N atoms and optionally mono- to tetra-substituted by $R<2>$, $R<3>$, F, Cl, Br, I, NO_2 and OH; Y = bond or $NR<2>$; $R<1> = NR<2>C(=NR<2>)R<2>$, $C(=NR<2>)NR<2>R<3>$, $NR<2>C(=NR<2>)NR<2>R<3>$ or a 4-10 membered monocyclic or polycyclic aromatic or non-aromatic ring optionally containing 1-4 N, O and/or S atoms and optionally substituted by 1 or more $R<11>$, $R<12>$, $R<13>$ and $R<14>$; $R<2>$, $R<3> = H$, 1-10C alkyl (optionally substituted by 1 or more F), 3-12C cycloalkyl, 3-12C cycloalkyl-1-8C alkanediyl, 5-14C aryl, 5-14C aryl-1-8C alkanediyl, NH_2 , $R<7>N(R<8>)$ OR<8>, $R<7>OR<8>$, $R<7>COOR<8>$, $R<7>-5-14C$ arylene- $R<8>$, $R<7>NR<8>R<8>$, $R<7>NR<8>-1-8C$ hydroxyalkyl, $R<7>CONR<8>R<8>$, $R<7>NR<8>C(O)R<8>$, $R<7>COR<8>$, $C(=NR<8>)NR<8>R<8>$ or 1-18C alkylcarbonyloxy-1-6C alkanediyloxy carbonyl; $R<4> = R<7>QR<6>$, $R<7>OCOR<6>$, $R<7>COOR<6>$, $R<7>-5-14C$ arylene- $R<6>$, $R<7>NR<2>R<6>$, $R<7>NR<6>R<8>$, $R<7>OCONR<2>R<6>$, $R<7>NR<2>S(O)nR<6>$, $R<7>NR<2>COQR<6>$, $R<7>NR<2>C(O)R<6>$, $R<7>N(R<2>)C(O)N(R<2>)R<6>$, $R<7>N(R<2>)S(O)nN(R<2>)R<6>$, $R<7>S(O)nR<6>$, $R<7>C(O)R<6>$, $R<7>CONR<2>R<6>$, $R<7>S(O)nNR<2>R<6>$, Cy or 1-8C alkyl substituted by Cy; Cy = monocyclic or polycyclic, saturated or mono- or poly-unsaturated 10-18C cycloalkyl optionally substituted by 1 or more Z'; Z' = 1-10C alkyl (optionally substituted by 1 or more F), 3-12C cycloalkyl, 3-12C cycloalkyl-1-8C alkanediyl, 5-14C aryl, 5-14C aryl-1-8C alkanediyl, 1-8C alkoxy, 5-14C aryl-1-8C alkanediyloxy, 5-14C aryloxy, 1-8C alkylcarbonyloxy-1-4C alkanediyloxy, NH_2 , $NH(1-8C$ alkyl), $N(1-8C$ alkyl) $_2$, 5-14C aryl-1-8C alkanediyamino, 5-14C arylamino, =Q, NO_2 , OH, F, Cl, Br or I; $R<5> = H$, F, 1-8C alkyl (optionally substituted by 1 or more F), 3-12C cycloalkyl, 3-12C cycloalkyl-1-8C alkanediyl, 5-14C aryl or 5-14C aryl-1-8C alkanediyl; $R<6> = Cy$ or 1-8C alkyl substituted by Cy; $R<7> = bond$ or 1-8C alkanediyl; $R<8> = H$, 1-8C alkyl (optionally substituted by 1 or more F, or one 3-12C cycloalkyl or 5-14C aryl), 3-12C cycloalkyl or 5-14C aryl; $R<9> = C(Q)R<10>$, $S(O)nR<10>$, $P(O)(R<10>)n$ or a 4-8 membered saturated or unsaturated heterocycle containing 1-4 N, O and/or S atoms; $R<10> = OH$, 1-8C

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Chandrakumar et al.
Reference 7

alkoxy(optionally substituted by 5-14C-aryl), 5-14C aryloxy, 1-8C alkylcarbonyloxy-1-4C alkanediylloxy, 5-14C aryl-1-8C alkanediylcarbonyloxy-1-6C alkanediylloxy, NH₂, mono- or di- 1-8C alkylamino, 5-14C aryl-1-8C alkanediylamino, 1-8C dialkylaminocarbonylmethyleneoxy, 5-14C aryl-1-8C dialkylaminocarbonylmethyleneoxy, 5-14C arylamino or the residue of a L- or D-amino acid; R<11>-R<14> = H, 1-10C alkyl (optionally substituted by 1 or more F), 3-12C cycloalkyl, 3-12C cycloalkyl-1-8C alkanediyl, 5-14C aryl, 5-14C aryl-1-8C alkanediyl, NH₂, R<7>N(R<8>)OR<8>, R<7>OR<8>, R<7>COOR<8>, R<7>NR<8>R<8>, R<7>NR<2>-1-8C hydroxyalkyl, R<7>CONR<2>R<8>, R<7>COR<8>, NR<2>C(=NR<2>)NR<2>R<3>, C(=NR<2>)NR<2>R<3>, R<7>-5-14C arylene-R<8>, R<7>NR<2>COR<8> or Q; n = 1 or 2; q = 0 or 1.

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